US Army Medical Research and Materiel

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Substituted Aromatic Compounds for Treatment of Antibiotic Resistant Infections

Features and advantages:

- **Some compounds are effective against antibiotic resistant organisms, *in vitro***
- **Some compounds are effective against *Plasmodium spp., in vivo***
- **Potentially effective against both Gram positive and Gram negative organisms**
- **Many compounds are lipophilic**

This invention provides compounds that could be used to treat infectious diseases which are resistant to conventional antibiotics. Some of the compounds have previously been used to treat malaria, while others are newly discovered. Most of the compounds are lipophilic, which should permit the drugs to enter into cells, including those of the central nervous system. Many of the compounds could be absorbed from the intestinal tract when given orally. Preferred compositions contain aryl ring systems, including phenyl, naphthyl and anthracene ring systems, substituted by a carbon bound to an oxygen which is also bound to a nitrogen through a saturated carbon or carbon chain. The saturated carbon or carbon chain may be substituted with halo, hydroxy, alkoxy, amino or alkylamino substituents.

The compounds could potentially be used to treat patients suffering from infections caused by either Gram positive or Gram negative organisms. The organisms could include antibiotic resistant strains of *Streptococcus*, *Staphylococcus*, *Bacillus anthracis*, *Neisseria*, various types of yeasts, and *Mycobacteria*. Suggested formulations include capsules for oral administration, gels for skin application, sprays for use in the oral-pharyngeal cavity, and a composition for intravenous administration comprising desbutylhalofantrin and glucose in normal saline. The later could prove valuable for administration intravenously during heart surgery and to patients suffering from endocarditis.

Some compounds were shown to be effective *in vitro* against antibiotic resistant strains of *Staphylococcus* [illegible] and *Mycobacteria.* Desbutylhalofantrin has been found superior to halofantrine for the treatment of malaria.

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Point of Contact

Dr. Paul C. Mele
Director, Office of Research and Technology Applications
USAMRMC, MCMR-ZA-J
504 Scott St., Ft. Detrick, MD 21702-5012
E-mail: usamrmcorta@amedd.army.mil
Voice: 301-619-6664/2065/7219 Fax: 301-619-5034

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